Self-renewal and multilineage differentiation in vitro from murine prostate stem cells.

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Public Summary:

Scientific Abstract:

Murine prostate stem cells express integrin alpha 6, which modulates survival, proliferation, and differentiation signaling through its interaction with the extracellular protein laminin. When plated in vitro in laminin containing Matrigel medium, 1 of 500-1,000 murine prostate cells can grow and form clonogenic spheroid structures that we term prostate spheres. Prostate spheres can be serially passaged individually or in bulk to generate daughter spheres with similar composition, demonstrating that sphere-forming cells are capable of self-renewal. Spheres spontaneously undergo lineage specification for basal and transit-amplifying cell types. P63-expressing cells localized to the outer layers of prostate spheres possess higher self-renewal capacity, whereas cells toward the center display a more differentiated transit-amplifying phenotype, as demonstrated by the expression of the prostate stem cell antigen. When dihydrotestosterone is added to the medium, the androgen receptor is stabilized, is imported to the nucleus, and drives differentiation to a luminal cell-like phenotype. A fraction of sphere cells returned to an in vivo environment can undergo differentiation and morphogenesis to form prostate tubular structures with defined basal and luminal layers accompanied by prostatic secretions. This study demonstrates self-renewal and multilineage differentiation from single adult prostate stem/progenitor cells in a specific in vitro microenvironment.

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